NIOSH Skin Notation Profiles

2-Ethoxyethyl Acetate

SK

- ID^{SK}
- [~~SK~~]
- SYS
- SYS (FATAL)
- DIR
- DIR (IRR)
- DIR (COR)
- SEN

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

NIOSH Skin Notation (SK) Profiles

2-Ethoxyethyl Acetate
[CAS No. 111-15-9]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
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National Institute for Occupational Safety and Health

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Foreword

As the largest organ of the body, the skin performs multiple critical functions, such as serving as the primary barrier to the external environment. For this reason, the skin is often exposed to potentially hazardous agents, including chemicals, which may contribute to the onset of a spectrum of adverse health effects ranging from localized damage (e.g., irritant contact dermatitis and corrosion) to induction of immune-mediated responses (e.g., allergic contact dermatitis and pulmonary responses), or systemic toxicity (e.g., neurotoxicity and hepatoxicity). Understanding the hazards related to skin contact with chemicals is a critical component of modern occupational safety and health programs.

In 2009, the National Institute for Occupational Safety and Health (NIOSH) published Current Intelligence Bulletin (CIB) 61 – A Strategy for Assigning New NIOSH Skin Notations [NIOSH 2009-147]. This document provides the scientific rationale and framework for the assignment of multiple hazard-specific skin notations (SK) that clearly distinguish between the systemic effects, direct (localized) effects, and immune-mediated responses caused by skin contact with chemicals. The key step within assignment of the hazard-specific SK is the determination of the hazard potential of the substance, or its potential for causing adverse health effects as a result of skin exposure. This determination entails a health hazard identification process that involves use of the following:

- Scientific data on the physicochemical properties of a chemical
- Data on human exposures and health effects
- Empirical data from *in vivo* and *in vitro* laboratory testing
- Computational techniques, including predictive algorithms and mathematical models that describe a selected process (e.g., skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for 2-Ethoxyethyl acetate (2-EEA). In particular, this document evaluates and summarizes the literature describing the hazard potential of the substance and its assessment according to the scientific rationale and framework outlined in CIB 61. In meeting this objective, this *Skin Notation Profile* intends to inform the audience—mostly occupational health practitioners, researchers, policy- and decision-makers, employers, and workers in potentially hazardous workplaces—so that improved risk-management practices may be developed to better protect workers from the risks of skin contact with the chemicals of interest.

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Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
CIB	Current Intelligence Bulletin
cm^2	square centimeter(s)
cm/hr	centimeter(s) per hour
DEREK	Deductive Estimation of Risk from Existing Knowledge
DIR	skin notation indicating the potential for direct effects to the skin following contact with a chemical
EC	European Commission
2-EEA	2-ethoxyethyl acetate
EEC	European Economic Communities
GHS	Globally Harmonized System for Classification and Labelling of Chemicals
GPMT	guinea pig maximization test
IARC	International Agency for Research on Cancer
(IRR)	subnotation of SK: DIR indicating the potential for a chemical to be a skin irritant following exposure to the skin
k_{aq}	coefficient in the watery epidermal layer
k_p	skin permeation coefficient
k_{pol}	coefficient in the protein fraction of the stratum corneum
k_{psc}	permeation coefficient in the lipid fraction of the stratum corneum
LD_{50}	dose resulting in 50% mortality in the exposed population
LD_{Lo}	dermal lethal dose
LOAEL	lowest-observed-adverse-effect level
log K_{OW}	base-10 logarithm of a substance's octanol–water partition
M	molarity
m^3	cubic meter(s)
mg	milligram(s)
mg/cm^2-hr	milligram(s) per square centimeters per hour
mg/cm^3	milligram(s) per cubic centimeter
mg/kg	milligram(s) per kilogram body weight
mL	milliliter(s)
mL/kg	milliliter(s) per kilogram body weight
MW	molecular weight
NIOSH	National Institute for Occupational Safety and Health
nmole/cm^2-min	nanomoles per square centimeters per minute
NOAEL	no-observed-adverse-effect level
NTP	National Toxicology Program
OEL	occupational exposure limit

OSHA	Occupational Safety and Health Administration
REL	recommended exposure limit
RF	retention factor
SEN	skin notation indicating the potential for immune-mediated reactions following exposure of the skin
SI ratio	ratio of skin dose to inhalation dose
SK	skin notation
S_W	solubility
SYS	skin notation indicating the potential for systemic toxicity following exposure of the skin
USEPA	United States Environmental Protection Agency

Glossary

Absorption—The transport of a chemical from the outer surface of the skin into both the skin and systemic circulation (including penetration, permeation, and resorption).

Acute exposure—Contact with a chemical that occurs once or for only a short period of time.

Cancer—Any one of a group of diseases that occurs when cells in the body become abnormal and grow or multiply out of control.

Contaminant—A chemical that is (1) unintentionally present within a neat substance or mixture at a concentration less than 1.0% or (2) recognized as a potential carcinogen and present within a neat substance or mixture at a concentration less than 0.1%.

Cutaneous (or percutaneous)—Referring to the skin (or through the skin).

Dermal—Referring to the skin.

Dermal contact—Contact with (touching) the skin.

Direct effects—Localized, non-immune-mediated adverse health effects on the skin, including corrosion, primary irritation, changes in skin pigmentation, and reduction/disruption of the skin barrier integrity, occurring at or near the point of contact with chemicals.

Immune-mediated responses—Responses mediated by the immune system, including allergic responses.

Sensitization—A specific immune-mediated response that develops following exposure to a chemical, which, upon re-exposure, can lead to allergic contact dermatitis (ACD) or other immune-mediated diseases such as asthma, depending on the site and route of re-exposure.

Substance—A chemical.

Systemic effects—Systemic toxicity associated with skin absorption of chemicals after exposure of the skin.

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1 Introduction

1.1 General Substance Information

Chemical: 2-Ethoxyethyl acetate (2-EEA)

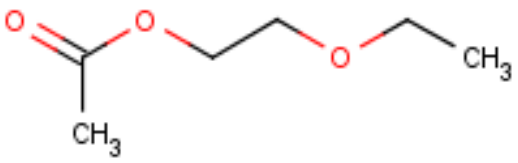
CAS No: 111-15-9

Molecular weight (MW): 132.2

Molecular formula:

CH3COOCH2CH2OC2H6

Structural formula:



Synonyms:

2-EEA; Cellosolve® acetate; EGMEA; Ethylene glycol monoethyl ether acetate; Glycol monoethyl ether acetate

Uses:

2-Ethoxyethyl acetate (2-EEA) is used as a solvent and chemical intermediate.

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with 2-EEA and (2) the rationale behind the hazard-specific skin notation (SK) assignment for 2-EEA. The SK assignment is based on the scientific rationale and logic outlined in the *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009]. The summarized information and health hazard assessment are limited to an evaluation of the potential health effects of dermal exposure to 2-EEA. A literature search was conducted through April 2014 to identify information on 2-EEA, including but not limited to data relating to its toxicokinetics, acute toxicity, repeated-dose systemic toxicity, carcinogenicity, biological system/function–specific effects (including reproductive and developmental effects and immunotoxicity), irritation, and sensitization. Information was considered from studies of humans, animals, or appropriate modeling systems that are relevant to assessing the effects of dermal exposure to 2-EEA.

1.3 Overview of SK Assignment

2-EEA is potentially capable of causing adverse systemic health effects following skin contact. A critical review of available data has resulted in the following SK assignment for 2-EEA: **SK: SYS.** Table 1 provides an overview of the critical effects and data used to develop the SK assignment for 2-EEA.

Table 1. Summary of the SK assignment for 2-EEA

Skin notation	Critical effect	Available data
SK: SYS	Maternal and developmental toxicity	Limited animal data

2 Systemic Toxicity from Skin Exposure (SK: SYS)

Limited toxicokinetic data were identified that estimated the percent absorption of 2-EEA following dermal exposure in humans or animals *in vivo* or *in vitro*. However, percutaneous absorption studies were identified that measured permeability constants and/or rate of absorption of 2-EEA in animals *in vivo* and *in vitro* and in humans *in vitro*. For example, in an *in vivo* test Guest et al. [1984] applied 15 milliliters (mL) of undiluted, radiolabeled 2-EEA to the thorax of dogs for 30 or 60 minutes and estimated the absorption rate to be 110 nanomoles per square centimeters per minute (nmole/cm^2-min) [corresponding to 0.87 mg/cm^2-hr]. Dugard et al. [1984] measured the absorption of 2-EEA, after application of 1 mL for 8 hours (hr) to the isolated human abdominal epidermis. The authors reported a permeability constant of 8.07 x 10^4 cm/hr and an absorption rate of 0.8 milligrams per square centimeters per hour (mg/cm^2-hr), with a lag time of less than 1 hr. Barber et al. [1992] reported an absorption rate of 1.41 mg/cm^2-hr and a permeability constant of 1.45 x 10^{-3} cm/hr when undiluted 2-EEA was applied to isolated human stratum corneum *in vitro* for 8 hr. Using full thickness rat skin *in vitro*, Barber et al. [1992] estimated an absorption rate of 2.41 mg/cm^2-hr and permeability constant of 2.47 x 10^{-3} cm/hr following application of undiluted 2-EEA for 8 hr using full thickness rat skin *in vitro*. Guest et al. [1984] also performed *in vitro* tests in which 0.3 mL of radiolabeled 2-EEA was applied to the skin from the thorax of necropsied beagles and absorption rates were measured hourly from 2 to 7 hr after application. The estimated percutaneous absorption rate was 279.7 nmole/cm^2-min [corresponding to 2.22 mg/cm^2-hr].

The potential of 2-EEA to pose a skin absorption hazard was also evaluated, with use of a predictive algorithm for estimating and evaluating the health hazards of dermal exposure to substances [NIOSH 2009]. The evaluation method compares an estimated dose accumulated in the body from skin absorption and an estimated dose from respiratory absorption associated with a reference occupational exposure limit. On the basis of this algorithm, a ratio of the skin dose to the inhalation dose (SI ratio) of 0.003 was calculated for 2-EEA. An SI ratio of ≥0.1 indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, 2-EEA is not considered to be absorbed through the skin following dermal exposure using only the SI ratio. However, Shih et al. [2009] found that 2-EEA on the skin was strongly associated with airborne 2-EEA, indicating that airborne 2-EEA needs to be considered when assessing dermal exposure. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

No estimate of the dermal lethal doses (LD_{Lo}) of 2-EEA for humans was identified. Reported dermal LD_{50} (lethal dose in 50% of exposed animals) values ranged from 10300 milligrams per kilogram body weight (mg/kg) in rabbits to 18800 mg/kg in guinea pigs when applied under occlusion [Carpenter 1947]. The acute dermal LD_{50} values for 2-EEA in rabbits and guinea pigs are greater than the critical dermal LD_{50} value of 2000 mg/kg body weight that identifies chemical substances with the potential for acute dermal toxicity [NIOSH 2009], indicating that 2-EEA is not acutely toxic following dermal exposure.

No epidemiological or occupational case reports or repeated-dose, subchronic, or chronic toxicity studies in animals were identified that evaluated the potential of 2-EEA to cause systemic effects following dermal exposure.

Specialty studies were identified that evaluated biological system/function specific effects, such as reproduction and developmental effects following dermal exposure to 2-EEA. Hardin et al. [1984] applied 0.35 mL of pure, undiluted 2-EEA to adult rats 4 times per day, for a total daily dose of 1.4 mL [corresponding to 1365 mg/day], on days 7 to 16 of gestation. Based on the average body weight

provided on gestation days 5, 7, 12, 17, and 21, an average daily body weight of approximately 234 grams was estimated, giving a dose of 5830 mg/kg-day of 2-EEA. Compared to water controls, treatment with 2-EEA caused maternal toxicity that manifested as significant reductions in maternal body weight gain, gravid uterus weights, and extragestational body weight gains. 2-EEA was also embryotoxic, as reflected in significantly higher frequencies of completely resolved litters, significantly increased number of dead implants per litter, significantly reduced number of live fetuses per litter, significantly reduced body weight of live fetuses, and significantly increased total cardiovascular malformations and skeletal variations (total ribs, vertebrae, and reduced ossification variations) [Hardin et al. 1984]. A Lowest Observed Adverse Effect Level (LOAEL) of 5830 mg/kg-day, the only dose tested, for maternal and developmental toxicity can be established from this study. 2-EEA is expected to be readily hydrolyzed *in vivo* to 2-ethoxyethanol and acetate [Hardin et al. 1984; ACGIH 2001b]. In the Hardin et al. [1984] study, at equimolar doses of 2-EEA and 2-ethoxyethanol, 2-EEA caused even more severe maternal, embryo, and fetal toxicity than did 2-ethoxyethanol. In an earlier study, Hardin et al. [1982] observed significant increase in resorptions, decreases in number of live fetuses per litter, decreases in fetal body weight, and an increase in the incidence of visceral malformations (predominantly of the cardiovascular system) and skeletal variations in rats dermally exposed 4 times/day to 0.25 mL/application of 2-ethoxyethanol [corresponding to 1 mL/day] and intrauterine death in rats dermally exposed 4 times/day to 0.50 mL/application of 2-ethoxyethanol [corresponding to 2 mL/day] during gestation days 7 to 16, followed by a 5-day post exposure period. A LOAEL of 3445 mg/kg-day, derived from the group that received 1 mL/day, for developmental effects can be established in the absence of maternal toxicity from these studies [Hardin et al. 1982, 1984]. 2-EEA is considered a potential reproductive and developmental toxicant following repeated dermal exposure.

Use of the developmental toxicity studies by Hardin et al. [1982, 1984] to determine whether dermal application of 2-EEA is a systemic toxicant is hindered by dosing regimen, since a LOAEL was identified at the only dose tested. Therefore, these studies do not indicate whether 2-EEA causes such effects at doses below 1000 mg/kg body weight that identifies chemicals with systemic toxicity potential following repeated dermal administration.

No specialty studies evaluating immunotoxicity following dermal exposure were identified. No epidemiological studies or animal bioassays were identified that evaluated the potential of 2-EEA to be a carcinogen following dermal exposure. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for 2-EEA.

No epidemiological studies, occupational exposure studies or repeat-dose or long-term studies in animals were identified for dermal exposure to 2-EEA. However, i*n vitro* evaluations of the skin permeability of 2-EEA **[Dugard et al. 1984; Barber et al. 1992]** * indicate that it is readily absorbed by the skin. Toxicity studies indicate 2-EEA is not acutely toxic following dermal exposure; however, developmental toxicity studies that utilized high dermal doses of 2-EEA showed the potential of the substance to cause maternal and developmental toxicity **[Hardin et al. 1984]**. Therefore, on the basis of the data for this assessment, 2-EEA is assigned the SK: SYS notation.

3 Direct Effects on Skin (SK: DIR)

No human or animal data on corrosivity of 2-EAA or *in vitro* tests for corrosivity using human or animal skin models or *in vitro* tests of skin integrity using cadaver skin were

*References in **bold** text indicate studies that serve as the basis of the SK assignments.

Table 2. Summary of the carcinogenic designations* for 2-EEA by numerous governmental and nongovernmental organizations

Organization	Carcinogenic designation
NIOSH [2005]	No designation
NTP [2011]	No designation
USEPA [2014]	No designation
European Parliament [2008]	No designation
IARC [2007]	No designation
EC [2014]†	No designation
ACGIH [2001a]	No designation

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; IARC = International Agency for Research on Cancer; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; USEPA = United States Environmental Protection Agency.
*The listed cancer designations were based on data from nondermal (such as oral or inhalation) exposure rather than dermal exposure.
†Date accessed.

identified. Truhaut et al. [1979] tested the irritancy of 2-EEA using the Draize method and found very slight erythema in 2 of 6 rabbits at 24 hours, but no irritation was observed after 72 hours, even in previously affected animals. Zissu et al. [1995] tested 3 rabbits using the European Economic Communities (EEC) methods and 6 rabbits using the Draize protocol. The authors found 2-EEA to be a nonirritant using the EEC test and to be slightly irritating using the Draize protocol. Zissu [1995] suggested that the slight irritation observed using the Draize protocol was due to the extended exposure period of 24 hours in the Draize test compared to the shorter exposure of 4 hours in the EEC test. The authors placed greater weight on the EEC protocol than on the Draize test results, based on the consideration that 24 hours continuous exposure is not representative of a potential human occupational exposure scenario.

The overall data indicate that at most, 2-EEA is a mild irritant. The effects are rapidly reversible and the appearance of irritation is dependent on the duration of exposure. This assessment is for occupational scenarios with daily exposures (typically 8 to 12 hours) intermediate between a duration that causes mild irritation (24 hours) and a duration that does not cause irritation (4 hours). Based on the minimal irritation observed even at 24 hours with constant contact, the weight of evidence from standard skin irritation tests suggests that 2-EEA is not likely to be a significant skin irritant in typical workplace scenarios. Therefore, on the basis of the data for this assessment, 2-EEA is not assigned the SK: DIR notation.

4 Immune-mediated Responses (SK: SEN)

No occupational exposure studies or diagnostic (human patch) studies were identified that investigated the skin sensitization potential of 2-EEA in humans. Zissu [1995] conducted a Magnusson Kligman [guinea pig maximization test (GPMT)] on 30 guinea pigs (10 guinea pigs were controls and 20 guinea pigs were treated). Using a 10% concentration as the challenge, the authors found no evidence of skin sensitization. Based on the results of the single GPMT available that indicate that 2-EEA is not a potential skin sensitizer, 2-EEA is not assigned the SK: SEN notation.

Table 3. Summary of previous skin hazard designations for 2-EEA

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption
OSHA [2006]	[skin]: Potential for dermal absorption
ACGIH [2001a]	[skin]: Potential for dermal absorption
EC [2014]*	R21: Harmful if in contact with skin

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration.
*Date accessed.

5 Summary

Toxicokinetic studies were identified for 2-EEA, but percent absorption estimates were not available. *In vitro* evaluation of the skin permeability of 2-EEA **[Dugard et al. 1984; Barber et al. 1992]** indicates the chemical is readily absorbed. No epidemiological or occupational exposure studies were identified that evaluated the potential of 2-EEA to cause systemic effects following dermal exposure. 2-EEA is not acutely toxic following dermal exposure; however, repeat-dose developmental toxicity studies identified in animals that employed high dermal doses resulted in maternal and developmental effects [**Hardin et al. 1984**]. The weight of evidence from standard irritation tests indicates that 2-EEA is not likely to be a skin irritant under typical workplace scenarios. Limited data from a predictive test (GPMT) indicate that 2-EEA is not a skin sensitizer. Therefore, on the basis of these assessments, 2-EEA is assigned a composite skin notation of **SK: SYS.**

Table 3 summarizes the skin hazard designations for 2-EEA previously issued by NIOSH and other organizations. The equivalent dermal designation for 2-EEA, according to the Global Harmonization System (GHS) of Classification and Labelling of Chemicals, is Acute Toxicity Category 4 (Hazard statement: Harmful in contact with the skin) [European Parliament 2008]. 2-EEA has also been classified as a Reproductive Toxicity Category 2 (Hazard statement: Suspected of damaging fertility or the unborn child) [European Parliament 2008].

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Note: Asterisks (*) denote sources cited in text; daggers (†) denote additional resources.

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Appendix: Calculation of the SI Ratio for 2-EEA

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for 2-EEA. Although the SI ratio is considered in the determination of a substance's hazard potential following skin contact, it is intended only to serve as supportive data during the assignment of the NIOSH SK. An in-depth discussion on the rationale and calculation of the SI ratio can be found in Appendix B of the *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009].

Overview

The SI ratio is a predictive algorithm for estimating and evaluating the health hazards of skin exposure to substances. The algorithm is designed to evaluate the potential for a substance to penetrate the skin and induce systemic toxicity [NIOSH 2009]. The goals for incorporating this algorithm into the proposed strategy for assigning SYS notation are as follows:

1. Provide an alternative method to evaluate substances for which no clinical reports or animal toxicity studies exist or for which empirical data are insufficient to determine systemic effects.
2. Use the algorithm evaluation results to determine whether a substance poses a skin absorption hazard and should be labeled with the SYS notation.

The algorithm evaluation includes three steps:

1. determining a skin permeation coefficient (k_p) for the substance of interest,
2. estimating substance uptake by the skin and respiratory absorption routes, and
3. evaluating whether the substance poses a skin exposure hazard.

The algorithm is flexible in the data requirement and can operate entirely on the basis of the physicochemical properties of a substance and the relevant exposure parameters. Thus, the algorithm is independent of the need for biologic data. Alternatively, it can function with both the physicochemical properties and the experimentally determined permeation coefficient when such data are available and appropriate for use.

The first step in the evaluation is to determine the k_p for the substance to describe the transdermal penetration rate of the substance [NIOSH 2009]. The k_p, which represents the overall diffusion of the substance through the stratum corneum and into the blood capillaries of the dermis, is estimated from the compound's molecular weight (MW) and base-10 logarithm of its octanol–water partition coefficient (log K_{ow}). In this example, k_p is determined for a substance with use of Equation 1. A self-consistent set of units must be used, such as outlined in Table A1. Other model-based estimates of k_p may also be used [NIOSH 2009].

Equation 1: Calculation of Skin Permeation Coefficient (kp)

$$k_p = \frac{1}{\frac{1}{k_{psc} + k_{pol}} + \frac{1}{k_q}}$$

Where k_{psc} is the permeation coefficient in the lipid fraction of the stratum corneum, k_{pol} is the coefficient in the protein fraction of the stratum corneum, and k_{aq} is the coefficient in the watery epidermal layer. These components are individually estimated by

$$\log k_{psc} = -1.326 + 0.6097 \times \log K_{ow} - 0.1786 \times MW^{0.5}$$

$$k_{pol} = 0.0001519 \times MW^{-0.5}$$

$$k_{aq} = 2.5 \times MW^{-0.5}$$

The second step is to calculate the biologic mass uptake of the substance from skin absorption (skin dose) and inhalation (inhalation dose) during the same period of exposure. The skin dose is calculated as a mathematical product of the k_p, the water solubility (S_w) of the substance, the exposed skin surface area, and the duration of exposure. Its units are milligrams (mg). Assume that the skin exposure continues for 8 hours to unprotected skin on the palms of both hands (a surface area of 360 square centimeters [cm^2]).

Equation 2: Determination of Skin Dose

$$\text{Skin dose} = k_p \times S_w \times \text{Exposed skin surface area} \times \text{Exposure time}$$

$$= k_p(\text{cm/hour}) \times S_w\ (\text{mg/cm}^3) \times 360\ \text{cm}^2 \times 8\ \text{hours}$$

The inhalation dose (in mg) is derived on the basis of the occupational exposure limit (OEL) of the substance—if the OEL is developed to prevent the occurrence of systemic effects rather than sensory/irritant effects or direct effects on the respiratory tract. Assume a continuous exposure of 8 hours, an inhalation volume of 10 cubic meters (m^3) inhaled air in 8 hours, and a factor of 75% for retention of the airborne substance in the lungs during respiration (retention factor, or RF).

Equation 3: Determination of Inhalation Dose

$$\text{Inhalation dose} = \text{OEL} \times \text{Inhalation volume} \times \text{RF}$$

$$= \text{OEL}\ (\text{mg/m}^3) \times 10\ \text{m}^3 \times 0.75$$

The final step is to compare the calculated skin and inhalation doses and to present the result as a ratio of skin dose to inhalation dose (the SI ratio). This ratio quantitatively indicates (1) the significance of dermal absorption as a route of occupational exposure to the substance and (2) the contribution of dermal uptake to systemic toxicity. If a substance has an SI ratio greater than or equal to 0.1, it is considered a skin absorption hazard.

Calculation

Table A1 summarizes the data applied in the previously described equations to determine the SI ratio for 2-EEA. The calculated SI ratio was 0.003. On the basis of these results, 2-EEA is not predicted to represent a skin absorption hazard.

Appendix References

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Table A1. Summary of data used to calculate the SI ratio for 2-EEA

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hour	1.3432×10^{-3}
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hour	1.3211×10^{-5}
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hour	0.2174
Molecular weight (*MW*)*	amu	132.2
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})*	None	0.83
Calculated skin permeation coefficient (k_p)	cm/hour	1.3383×10^{-3}
Skin dose		
Water solubility (S_w)*	mg/cm^3	0.13
Calculated skin permeation coefficient (k_p)	cm/hour	1.3383×10^{-3}
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hour	8
Calculated skin dose	mg	0.5029
Inhalation Dose		
Occupational exposure limit (OEL)†	mg/m^3	24.17
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	181.28
Skin dose–to–inhalation dose (SI) ratio	None	0.003

*Variables identified from SRC [2009].

†The OEL used in calculation of the SI ratio for 2-EEA was the NIOSH recommended exposure limit (REL) [NIOSH 2005].

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